CLAIMS

1. A method for producing infectious hepacivirus-like particles *ex vivo* comprising the steps of:

- providing a first nucleic acid sequence comprising a packaging competent retroviral-derived genome;

- providing a second nucleic acid sequence comprising a cDNA encoding core proteins from said retrovirus;

- providing a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein;

- transfecting host cells with said nucleic acid sequences and maintaining the transfected cells in culture for sufficient time to allow expression of the cDNAs to produce structural proteins from hepacivirus and retrovirus; and allowing the structural proteins to form virus-like particles.

2. The method according to claim 1, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

3. The method according to claim 1 or 2, wherein said packaging competent retroviral-derived genome and core proteins are from a retrovirus selected from the group consisting of MLV, ALV, RSV, MPMV, HIV-1, HIV-2, SIV, EIAV, CAEV, or HFV.

4. The method according to claim 2 or 3, wherein said polyprotein comprises a hepacivirus core protein and a hepacivirus E1 protein.

5. The method according to any of claims 2 to 4, wherein said polyprotein comprises a hepacivirus core protein and a hepacivirus E2 protein.

6. The method according to any of claims 1 to 5, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a hepacivirus p7 protein.

7. The method according to any of claims 1 to 6, wherein said polyprotein comprises native hepacivirus E1 and/or E2 protein, and optionally native hepacivirus p7 protein.

8. The method according to any of claims 2 to 7, wherein said polyprotein comprises a native hepacivirus core protein, a native hepacivirus E1 protein and native hepacivirus E2 protein, and optionally a native p7 protein.

9. The method according to any of claims 2 to 8, wherein core protein, E1 protein and E2 protein, and optionally p7 protein, are derived from a same hepacivirus.

10. The method according to claim 9, wherein said hepacivirus is a hepatitis C virus (HCV).

11. The method according to claim 10, wherein said HCV core protein comprises the last 21 amino acids of the carboxy-terminus of HCV core.

12. The method according to claim 9 or 10, wherein said E2 protein is a mutated E2 protein selected from the group consisting of a E2 protein deleted from its C-terminal amino acid residue, and a native E2 protein wherein the hypervariable region 1 (HRV1) has been deleted.

13. The method according to any of preceding claims, wherein said nucleic acid sequence comprising a packaging competent retroviral-derived genome further comprises a transgene.

14. An infectious hepacivirus-like particle susceptible to be obtained by a method according to any of preceding claims, comprising the core proteins from a retrovirus, and a E1 hepacivirus glycoprotein and/or a E2 hepacivirus glycoprotein.

15. The infectious particle according to claim 14, comprising E1 and E2 hepacivirus glycoproteins.

16. The infectious particle according to claim 14, comprising E1 hepacivirus glycoprotein.

17. The infectious particle according to claim 14, comprising E2 hepacivirus glycoprotein.

18. The infectious particle according to any of claims 14 to 17, further comprising a hepacivirus p7 protein.

19. The infectious particle according to any of claims 14 to 18, comprising native E1 and/or E2 hepacivirus glycoprotein, and optionally native p7 protein.

20. The infectious particle according to any of claims 14 to 19, wherein core E1 and E2 protein, and optionally p7 proteins, are derived from a same hepacivirus.

21. The infectious particle according to claim 20, wherein said hepacivirus is HCV.

22. The infectious particle according to claim 21, wherein said E2 protein is a mutated E2 protein selected from the group consisting of a native E2 protein deleted from its C-terminal amino acid residue, and a native E2 protein wherein the hypervariable region 1 (HRV1) has been deleted.

23. The infectious particle according to any of claims 14 to 23, wherein said retrovirus is selected from the group consisting of MLV, ALV, RSV, MPMV, HIV-1, HIV-2, SIV, EIAV, CAEV, or HFV.

24. The infectious particle according to any of claims 14 to 23, wherein said nucleic acid sequence comprising a packaging competent retroviral-derived genome further comprises a transgene.

25. Use of three nucleic acid sequences for the preparation of a medicament useful as a vaccine against hepatitis, wherein the nucleic acid sequences are :

- a first nucleic acid sequence comprising a packaging competent retroviral-derived genome;

- a second nucleic acid sequence comprising a cDNA encoding core proteins from said retrovirus;

- a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein ;

and, when transferred into cells of a subject, the nucleic acids sequences allow the production of structural proteins from hepacivirus and retrovirus, wherein the structural proteins form virus-like particles that are immunogenic.

26. The use according to claim 25 wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

27. The use according to claim 25 or 26, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a hepacivirus p7 protein.

28. The use according to any of claims 25 to 27, wherein said hepacivirus is HCV.

29. A method for *ex vivo* identification of a receptor for hepacivirus E1 and/or E2 glycoprotein comprising detection of the binding of an infectious particle according to any of claims 14 to 23, to a cell receptor.

30. A method for *ex vivo* identifying a cell receptor for hepacivirus comprising the step consisting of:

- transfecting a cell which is not permissive for hepacivirus infection with a nucleic acid sequence encoding a protein likely to be a receptor for hepacivirus;
- contacting said transformed cell with a hepacivirus-like particle according to any of claims 14 to 23;
- determining whether said transformed cell has become permissive or not for hepacivirus infection; and
- identifying as a cell receptor for hepacivirus said protein expressed by the transformed cell that has become permissive.

31. A method for *ex vivo* identifying a cell receptor for a hepacivirus comprising the step consisting of:

- providing an expression cDNA library obtained from a cell permissive for hepacivirus infection;
- transfecting cells that are not permissive for hepacivirus infection with said expression cDNA library;
- contacting said transformed cells with hepacivirus -like particles according to any of claims 14 to 23;
- identifying and isolating those transformed cells that have become permissive for hepacivirus infection;
- isolating the expression vector transfected in cells that have become permissive; and
- identifying as a receptor for hepacivirus the proteins encoded by the cDNA sequence of said isolated expression vectors.

32. A method of *ex vivo* screening or identification of molecules capable of interfering with hepacivirus entry in cells comprising comparison of the level of cell infection by an infectious particle according to any of claims 14 to 23 in the presence or the absence of a candidate molecule.

33. A method of *in vitro* diagnosis of a hepacivirus infection in a patient, comprising detecting immune complexes formed by interaction of anti-hepacivirus antibodies likely to be present in a biological sample of the patient with hepacivirus-like particle according to any of claims 14 to 23.

34. A method of *in vitro* diagnosis of a hepacivirus infection in a patient, comprising detecting an inhibitory effect of anti-hepacivirus antibodies likely to be

present in a biological sample of the patient, on the infection of a permissive cell by hepacivirus-like particles according to any of claims 14 to 23.

35. A diagnostic kit useful for the method of claim 34, comprising a hepacivirus-like particle according to any of claim 14 to 23 and appropriate means of detection of said immune complexes.

36. Vaccine composition comprising a hepacivirus-like particle according to any of claims 14 to 24 and a pharmaceutically acceptable carrier.

37. A method for *in vitro* transferring a transgene of interest in a hepatic cell comprising infecting a cell with a hepacivirus-like particle as described in any of claims 14 to 24, wherein the hepacivirus-like particle carries a transgene of interest.

38. Use of a hepacivirus-like particle according to any of claims 14 to 24, that carries a transgene of interest, for the preparation of a medicament for the prevention or treatment of a disease in a patient, wherein the hepacivirus-like particle allows the transfer of the transgene of interest into a cell of the patient, and encodes a product that has a prophylactic or therapeutic effect against the disease.

39. A transformed host cell that contains :

- a first nucleic acid sequence comprising a packaging competent retrovirus-derived genome;

- a second nucleic acid sequence comprising a cDNA encoding the core proteins from said retrovirus; and

- a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

40. The transformed host cell according to claim 39 wherein said third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

41. The transformed host cell according to claim 39 or 40, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a HCV p7 protein.

42. The transformed host cell according to any of claims 39 to 41, wherein said hepacivirus is HCV.

43. A method of *ex vivo* screening of molecules capable of interfering with hepacivirus entry in cells comprising comparing the level of fusion of a transformed

host cell according to any of claims 39 to 42 to a target host cell, in the presence or the absence of a candidate molecule.

44. The method according to claim 43, comprising the steps consisting of:

- co-culturing said transformed host cell with a target host cell, in the absence or presence of a candidate molecule, under conditions that allow syncytia formation, *i.e.* cell-cell fusion, and hepacivirus-like particle entry in target host cell in the absence of any candidate molecule;

- assessing syncytia formation in the absence or in the presence of said candidate molecule;

- comparing syncytia formation measured in presence of said candidate molecule with syncytia formation measured in absence of any candidate molecule;

- identifying as a molecule capable of interfering with hepacivirus entry the candidate molecule for which syncytia formation, as measured in the presence of said molecule, is decreased as compared to syncytia formation measured in the absence of any candidate molecule.

45. The method, according to any of claims 29 to 34, 37, and 42 to 44, wherein said hepacivirus is HCV.